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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/568,246	07/28/2006	Alastair David Griffiths Lawson	13001011PCTUS	9639

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EXAMINER	
WEN, SHARON X	

ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
11/28/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/568,246	LAWSON ET AL.	
	Examiner	Art Unit	
	SHARON WEN	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 July 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,6,21 and 22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3, 6, 21, 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment, filed 07/21/2008, has been entered.

Claims 2, 4, 5 and 7-20 have been canceled.

Claims 1, 3, 6, 21 and 22 are pending and currently under examination as they read on a method of enriching a population of cells which produce an antibody.

2. This Action will be in response to Applicant's Arguments/Remarks, filed 07/21/2008.

The rejections of record can be found in the previous Office Action.

Specification

3. Applicant's amendment to the specification to correct trademarks, filed 07/21/2008, has been entered.

Claim Rejections - 35 USC § 112 first paragraph

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1, 3, 6 and newly added claims 21-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant's arguments, filed 07/21/2008, have been fully considered but have not been found convincing essentially for the reasons of record.

In response to Applicant's argument that the skilled artisan can readily determine which cell markers are "essentially unique" based on the definition for "essentially unique" provided in the specification, the following is noted.

"Essentially unique" is defined in the specification (page 3, lines 31-33) as follows:

"Essentially unique" includes a marker that is predominantly present on those cells capable of producing antibody compared to other cells types, *but not necessarily to the exclusion of all other cell types*. Hence, such a marker may also be present on one or two or even three or more other cell types.

The instant specification does not clearly define which cell markers are considered "predominantly present" on those antibody-producing cells, nor does the specification provide a standard to ascertain the degree of "predominant presence". Therefore, one skill in the art would not readily determine which cell markers are considered essentially unique that are predominantly present on the antibody-producing cells. Furthermore, as stated in the above definition, those "essentially unique" markers are not exclusive to the antibody-producing cells but are also found on other cell types. Therefore, the skilled artisan would not be able to determine which markers are essentially unique to the antibody-producing cells.

In response to Applicant's argument that the disclosed species of the markers, i.e., "CD5, CD9, CD10, CD19, CD20, CD21, CD22, CD45, CD45 RC" sufficiently provide written description for the entire genus broadly encompassed by the recitation of "a marker", the following is noted.

Given the plethora of cell surface markers and the non-limiting definition of these "essentially unique" markers, one skilled in the art cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus of the markers that exhibit this functional property because these species do not share a common structure drawn to a common function, i.e., essentially unique to antibody-producing cell. For example, CD45 is not limited to B cell, but also appears on T cell. Therefore the specification does not provide sufficient written support for the genus of markers recited in the claims.

Applicant's argument has been considered in full but not found convincing.

Therefore, the rejection of record is **maintained** for the reasons of record, as it applies to the amended and newly added claims. The rejection of record is incorporated by reference herein, as if reiterated in full.

Claim Rejections - 35 USC § 102

6. The previous rejection under 35 U.S.C. 102(b) as being anticipated by Chang (US Patent 5,213,960) has been withdrawn in view of Applicant's amendment, filed 07/21/2008.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1, 3, 6, and newly added claims 21-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chang (US Patent 5,213,960, reference of record) in view of Goldsby et al. (*Kuby Immunology*, 4th edition, 2000, W. H. Freeman and Co., New York, USA. Pages 104 and 165-169) and Brezinsky et al. (*J.I.M.* 2003, 277:141-155, reference of record, cited on IDS).

The following New Grounds of Rejection are necessitated by Applicant's amendment, filed 07/21/2008.

Chang taught an enrichment method using FACS comprising labeling a B cell marker with an antibody conjugated to a fluorescent label and the antigen of interest that was labeled with a second antibody conjugated to a fluorescent label (see entire document, in particular, see Abstract, Summary of the Invention and Claims 2-12).

In particular, Chang taught labeling a marker which is unique to B cells, e.g., CD19 or γ chain, κ or λ chains, and Fc receptor (see, e.g., column 5, lines 35-53 and claims 2-3 and 10-12) and also labeling the antibody that bound to the antigen of interest (see column 5, lines 25-34 and claim 1).

The difference between Chang and the present claims was that the Chang's antigen was directly labeled with a fluorochrome whereas the antigen recited in the present claims was indirectly labeled by a polyclonal antibody that recognized the antigen, wherein the polyclonal antibody was labeled with a fluorochrome.

However, it would have been obvious to one of ordinary skill in the art, at the time of the invention was made, to indirectly label the antigen with a polyclonal antibody because of the advantages offered by indirect labeling and polyclonal antibody as evidenced by Goldsby et al. (see entire document). In particular, Goldsby et al. taught that indirect labeling has the advantage of amplifying the fluorochrome signal because multiple labeled secondary antibodies can bind to a single primary antibody. Here, in the instant case, the recited "antigen" acts as the primary antibody that binds to the Ab-producing cell. Upon reading Goldsby, one of ordinary skill in the art would have readily appreciated using a polyclonal antibody as the flurorochrome-labeled secondary antibody because polyclonal antibodies are known to bind to multiple epitopes on a single antigen (as evidenced by Goldsby, see page 104, right column, last paragraph). Therefore, multiple fluorochrome-labeled polyclonal antibody can bind to a single antigen, thus amplifying the fluorochrome signal.

One of ordinary skill in the art would have been motivated to use polyclonal antibody as the labeling antibody to indirectly label the "antigen" because it would increase the sensitivity of the assay due to amplified signal.

Moreover, Chang differs from the present claims in that it does not explicitly teach "at least one wash step" in the enrichment method. However, it would have been obvious to a person of ordinary skill in the art to include at least one wash step in the method of enriching a population of cells using FACS because it is well known at the time of the invention to include wash steps in any immunoassays to increase specificity and decrease background noise.

For example, Brezinsky et al. teach washing antibody-producing cells before and after labeling in a method of enrichment FASC (see entire document, in particular, see page 143, paragraph bridging left and right columns).

Given that Chang teaches a washing solution in the assay (see column 11, lines 55-60) and that Brezinsky et al. also teach multiple washing steps in another FACS enrichment assay for antibody-producing cells, it would have been prima facie obvious to one of ordinary skill in the art to include the wash steps in the methods taught by the Chang reference.

One of skill in the art would have been motivated to wash the cells before and after labeling during the assays to reduce background signals.

Although, the prior arts do not explicitly teach the sequences of the method steps recited in the present claims, under the broadest reasonable interpretation of the claim, one of ordinary skill in the art would have immediately envisaged sequential steps upon reading the prior art because antibody labeling is known to be done in a step-wise fashion. Moreover, it would have been obvious to one of ordinary skill in the art to try, via routing experimentation, different sequences of these steps to achieve optimum sensitivity and specificity of the assay.

Therefore, the invention, as a whole, was *prima facie* obvious to one of ordinary skill in the art, at the time the invention was made as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

9. No claim is allowed.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHARON WEN whose telephone number is (571)270-3064. The examiner can normally be reached on Monday-Thursday, 8:30AM-6:00PM, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara can be reached on (571)272-0878. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sharon Wen/
Examiner, Art Unit 1644
November 13, 2008

/Phillip Gambel/
Phillip Gambel
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November 23, 2008